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**BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES**

Application Number: 10/801,277  
Filing Date: March 16, 2004  
Appellant(s): BROD, STALEY

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David L. Parker  
For Appellant

**EXAMINER'S ANSWER**

This is in response to the appeal brief filed 3/17/2008 appealing from the Office action mailed 9/18/2007.

**(1) Real Party in Interest**

A statement identifying the real party in interest is contained in the brief.

**(2) Related Appeals and Interferences**

The following are the related appeals, interferences, and judicial proceedings known to the examiner which may be related to, directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal:

Appeal No: 1999-2502 (Application No. 09/631, 470);

Appeal No: 2000-1094 (Application No. 08/946, 710).

**(3) Status of Claims**

The statement of the status of the claims contained in the brief is correct.

**(4) Status of Amendments**

The Appellant's statement of the status of amendments after final rejection contained in the brief is correct.

**(5) Summary of Claimed Subject Matter**

The summary of claimed subject matter contained in the brief is essentially correct.

**(6) Grounds of Rejection to be Reviewed on Appeal**

The Appellant's statement of the grounds of rejection to be reviewed on appeal is substantially correct. The changes are as follows:

**WITHDRAWN REJECTIONS**

The following grounds of rejection are not presented for review on appeal because they have been withdrawn by the examiner. The rejection of claims 19, 21-23 25-27 and 29-30 under 35 U. S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

It is noted that the Examiner rejected claims 19-22 under 35 U. S.C. 112, first paragraph and not claims 19-30 as indicated in the brief on page 7 (grounds of rejection to be reviewed on appeal).

The remainder of Appellant's statement of the grounds of rejection to be reviewed on appeal in the brief is correct.

**(7) Claims Appendix**

The copy of the appealed claims contained in the Appendix to the brief is correct.

**(8) Evidence Relied Upon**

Shiozawa *et al.* A preliminary study on the effect of alpha-interferon on the joint inflammation and serum calcium in rheumatoid arthritis (1992) British J. of Rheumatology, Vol. 31, pp.405-408.

Aman *et al.* Regulation of cytokine expression by interferon-alpha in human bone marrow stromal cells: inhibition of hemtopoietic growth factors and induction of interleukin-1 receptor antagonist (1994), Blood, Vol. 84, pp. 4142-4250.

Cummins, U. S. Patent No. 4, 497, 795, (issued Feb 5, 1985).

Cummins, U. S. Patent No. 5, 019, 382, (issued May 28, 1991).

**(9) Grounds of Rejection**

The following ground(s) of rejection are applicable to the appealed claims:

(A) Claim 20, 24 and 28 (not claim 30) are rejected under 35 U. S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear in claims 20, 24 and 28 the amount administered is in units or international units. The claims recite 30,000 units, but it is unclear if this should be "units" or "international units" because independent claims 19, 23 and 27 recite international units. Claims 20, 24 and 28 are dependent on claims 19, 23 and 27. Further, it is not clear if the dosage administered is per Kg or total dose administered.

(B) Claims 19-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification while enabling for treating destructive joint disease associated with rheumatoid arthritis in an individual or reducing inflammation associated with rheumatoid arthritis or reducing the level of interleukin in an individual with rheumatoid arthritis by oral administration of IFN- $\alpha$ , does not reasonably provide enablement for the preventing destructive joint disease associated with rheumatoid arthritis in an individual.

Claims 19-22 are drawn to preventing destructive joint disease associated with rheumatoid arthritis by administering IFN- $\alpha$  orally. Appellant has shown in general there is improvement in the clinical indices (page 81). The prior art also teaches there is improvement in the clinical indices (Shiozawa et al., 1992). However, the specification as filed is insufficient to enable one of skilled in the art to practice the claimed invention of preventing destructive joint disease associated with rheumatoid arthritis without an

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undue amount of experimentation because the specification and the prior art have not prevented destructive joint disease associated with rheumatoid arthritis by administering IFN- $\alpha$  orally.

Appellant has not disclosed how to use the claimed invention to prevent destructive joint disease associated with rheumatoid arthritis by administering IFN- $\alpha$  orally of the subjects. There is insufficient evidence of the invention with respect to the *in vivo* operability of the claimed invention. Specifically, specification and prior art only teach the improvement of clinical indices and not the preventing destructive joint disease associated with rheumatoid arthritis. For example, the specification fails to provide guidance with respect to what patient population will be selected for the preventing destructive joint disease associated with rheumatoid arthritis by administering IFN- $\alpha$ . Also if a patient population with the "disease symptoms" are identified, the onset of disease has taken place, thus the pathology cannot be prevented (only further progression maybe stopped).

Since, there is inadequate guidance as to the nature of the invention, it is merely an invitation to the artisan to use the current invention as a starting point for further experimentation for preventing destructive joint disease associated with rheumatoid arthritis by administering IFN- $\alpha$  orally. In addition, because there are no working examples provided describing prevention of diseases or models it would require an undue amount of experimentation to one of skill in the art to practice the claimed invention.

Given the breadth of claims 19-22 in light of the unpredictability of the art as determined by the lack of working examples, the level of skill of the artisan, and the lack of guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention for a method of preventing destructive joint disease associated with rheumatoid arthritis by administering IFN- $\alpha$  orally.

(C) Claims 19-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shozawa et al. (1992) in view of Cummings (U.S. Patent No: 4, 497, 795) and Cummings (U.S. Patent No: 5, 019, 382).

Shozawa et al. disclose the administration of interferon alpha to treat rheumatoid arthritis (Table II, page 406). There is a reduction in swelling (inflammation). The reference also teaches that interferon-alpha therapy improves certain inflammatory indices of rheumatoid arthritis such as the joint score, C-reactive protein value and platelet count (p.406, column 2). Thus treating the destructive joint disease associated with rheumatoid arthritis. The reference also teaches that cytokines such as interleukin-1 (IL-1), IL-6 and tumor necrosis factor  $\alpha$  play an important roles in the pathogenesis of rheumatoid arthritis (page 405). The reference does not teach dosage ranges described in the claims and the oral administration of IFN- $\alpha$ .

Cummings (U.S. Patent No: 4, 497, 795, Ref. A3 of PTO1449 dated 2/22/2005) teaches the oral administration of 5,000 to 50, 000 units of interferon per Kg body weight (see claim 15). This is equivalent to about 500 to 5000 IU/Kg. Cummings (U.S.

Patent No: 5, 019, 382, Ref. A4 of PTO1449 dated 2/22/2005) describes that 1 unit  $\cong$  0.1IU (column 3, lines 54-55). The reference also discloses a staggered regimen including one to three days treatment per week or month (column, 5, lines 53-55).

It would have been obvious to one of ordinary skill in the art, at the time the invention was made to modify the interferon doses of Shozawa et al. (1992) to those taught by Cummings (U.S. Patent No: 4, 497, 795) and Cummings (U.S. Patent No: 5, 019, 382) with expectation of treating rheumatoid arthritis patients. One of ordinary skill in the art would have been motivated to use interferon in the doses recommended by Cummings et al (U.S. Patent No: 4, 497, 795) to treat rheumatoid arthritis with the expectation of success as because Cummings (U.S. Patent No: 5, 019, 382) teaches the treatment of autoimmune disorder, which includes rheumatoid arthritis (see column 5, lines 40-50). Therefore, the instant claims are *prima facie* obvious over Shozawa et al. (1992) in view of Cummings (U.S. Patent No: 4, 497, 795) and Cummings (U.S. Patent No: 5, 019, 382).

(D) Claims 27-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shozawa et al. (1992) in view of Cummings (U.S. Patent No: 4, 497, 795) and Cummings (U.S. Patent No: 5, 019, 382) further in view of Aman et al. (1994).

The teachings of Shozawa et al. (1992) in view of Cummings (U.S. Patent No: 4, 497, 795) and Cummings (U.S. Patent No: 5, 019, 382) as been disclosed above in paragraph 10a. Although, Shozawa et al. teaches that cytokines such as interleukin-1 (IL-1), IL-6 and tumor necrosis factor  $\alpha$  play an important roles in the pathogenesis of



rheumatoid arthritis (page 405), it does not teach the reduction of interleukins following oral administration of interferon alpha.

Aman et al. (1994) teaches the reduction of interleukin-1 following the administration of Interferon alpha (see abstract, p.4147).

It would have been obvious to one of ordinary skill in the art, at the time the invention was made to modify the teaching of Shozawa et al. (1992), Cummings (U.S. Patent No: 4, 497, 795) and Cummings (U.S. Patent No: 5, 019, 382) with the teachings of Aman et al. (1994) with the expectation of reducing the level of interleukin in an individual with rheumatoid arthritis. One of ordinary skill in the art would have been motivated to use interferon to treat rheumatoid arthritis as taught by Shiozawa et al. (1992) in the doses recommended by Cummings et al (U.S. Patent No: 4, 497, 795 and U.S. Patent No: 5, 019, 382) to reduce the level of interleukin in an individual with rheumatoid arthritis with the expectation of success because Aman et al. (1994) teaches that the administration of interferon alpha will reduce interleukin-1. Therefore, the instant claims are *prima facie* obvious over Shozawa et al. (1992) in view of Cummings (U.S. Patent No: 4, 497, 795) and Cummings (U.S. Patent No: 5, 019, 382) further in view of Aman et al. (1994).

#### **(10) Response to Argument**

##### **A. Properly Constructed, The Claims are Definite**

Appellant argues the rejection of claims 20, 24 and 28 (not claim 30) under 35 U.S.C. 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter. Specifically, it is not clear in these claims whether

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the amount of IFN- $\alpha$  administered is in "units" or "international units", and whether the dosage administered is per kilogram of the subject, or total dose administered.

Appellant asserts that the meaning of the claims are discernable when construed under correct principles, including contents of the disclosure, teachings of the prior art and the claim interpretation that would be given by possessing the ordinary level of skill in the pertinent art at the time the invention was made. Appellant is arguing that the claims are construed in the proper context because the specification and prior art make it clear that claims 20, 24 and 28 (not 30) refer to the total dosage in international units (I.U). Instant specification on page 8, line 2-4 and page 21, lines 14-15 uses both "international units" (I.U) and "units" for administered dosage. Appellant cites prior art of U.S. Patent No. 5, 019, 382 column 3, lines 45-52 and U.S. Patent No. 4, 497, 795 column 4, lines 59-63 to suggest that both "international units" and "units" refers to the same quantity.

Although, Appellant uses "units" and "international units" interchangeably the '382 patent clearly contradicts Appellants position. It teaches that 1 unit is equivalent 0. 1 I.U (see column 3, lines 55-56). The '382 patent teaches that interferon of human and murine origins has been quantified in the art in terms of International Units ("IU").

Further, the '382 patent states that unit of interferon is to be distinguished from IU. In addition, '795 and '382 Patent discloses that "unit" as disclosed means the reciprocal of a dilution of interferon-containing material (column4, lines 63-65 and column 3, lines 45-56). Appellant also argues that construing the claims in the proper context of the specification and prior art makes clear that claims 20, 24 and 28 (not 30) do not refer to units per kilogram. However, independent claims 19, 23 and 27 from which claims 20,

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24 and 28 depend require orally administering about 50 I.U./kg to about 25, 000 I.U./kg of IFN- $\alpha$ . There is no teaching in the instant specification with respect to the conversion of the units. Appellant asserts that the Examiner's construction that 30,000 units could refer to 30,000 units/kg would result in improper dependent claims is not accurate. In fact claims 20, 24 and 28 lack antecedent basis for the disclosure of units. Further, the Office stated that it is not clear if the dosage administered (in units) is per Kg or total dose administered (see pages 3-4 of the Office Action dated 4/12/2007) because the dosage recited in the independent claim was for IU/kg. Thus, one possessing the ordinary level of skill in the pertinent art at the time the invention was made would interpret that "units" and "international units" recited in the instant claims are different measuring units.

#### **B. The Claimed Invention is Enabled by the Specification**

Appellant argues the rejection of claims 19-22 under 35 U.S.C. § 112, first paragraph under scope of enablement. The Office had previously indicated (Office Action of 4/12/2007 pages 4-6) that the specification, while enabling treating destructive joint disease associated with rheumatoid arthritis in an individual or reducing inflammation associated with rheumatoid arthritis or reducing the level of interleukin in an individual with rheumatoid arthritis by oral administration of IFN- $\alpha$ , does not reasonably provide enablement for the preventing destructive joint disease associated with rheumatoid arthritis in an individual.

Specifically, preventing destructive joint disease associated with rheumatoid arthritis in an individual is not enabled because the specification fails to provide

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guidance with respect to what patient population will be selected for the preventing of destructive joint disease associated with rheumatoid arthritis by administering IFN- $\alpha$ . In addition, if a patient population with the "disease symptoms" are identified, the onset of disease has taken place, thus the pathology cannot be prevented (only further progression maybe stopped). Further, the Office indicated that the prior art of Shiozawa et al. (1992) ("Shiozawa") teaches the treatment of the rheumatoid arthritis and not the prevention of destructive joint disease. Thus, meeting the minimal requirement of the examiner to give reasons for the uncertainty of the enablement per In re Bowen, 492 F.2d 859, 862-63, 181 USPQ 48, 51 (CCPA 1974). However, Appellant contends that it is not the case because Shiozawa reference fails to provide the Office any basis to question enablement in view of the guidance provided in the specification. Thus, Appellant contends that the Bowen requirement is not met by the Office. Contrary to Appellants assertions the Office maintains that the specification on page 85, lines 17-24 provides no guidance to the prevention of destructive joint disease because the speciation provides no teaching to identify a patient population which may be prevented from developing destructive joint disease. In fact the specification states that a proportion of RA patients will eventually develop destructive joint disease. It further states that the administration of IFN- $\alpha$  may prevent the destructive phase of the disease. The prior art of Shiozawa also teaches the treatment and not the prevention of destructive joint disease.

**1. The M. P. E. P. Requires a Reasonable, Sufficient Basis for Questioning Enablement**

The Appellant discusses the legal basis for questioning of the enablement by the Office. The Office takes no position on this discussion. However, the Office differs with Appellant's assertion that the Office has not provided sufficient, reasonable, specific or technical for reasons set forth in the Office Actions dated 4/12/2007, 9/18/2007 and discussed extensively in this Examiner's Answer.

## **2. What Shozawa Does not Teach Is Not Evidence of Non-enablement**

The Appellant asserts that the first reason for the Office to question enablement is because Shiozawa teaches treatment of rheumatoid arthritis, but not the prevention of destructive joint disease. Contrary to Appellant's assertion the Office Action mailed on 4/12/2007 (page 5) states that the specification and the prior art have not prevented (while treating these diseases) destructive joint disease associated with rheumatoid arthritis by administering IFN- $\alpha$  orally. Specifically, specification and prior art only teach the improvement of clinical indices and not the preventing destructive joint disease associated with rheumatoid arthritis. For example, the specification fails to provide guidance with respect to what patient population will be selected for the preventing destructive joint disease associated with rheumatoid arthritis by administering IFN- $\alpha$ . Although, the specification teaches that a portion of rheumatoid arthritis patients will develop destructive joint disease (page 85, lines 17-19) there is no guidance to identify this portion of the patient population. It is noted that claim 19 refers to an individual with an earlier stage of rheumatoid arthritis for preventing destructive joint disease but instant specification provides no clear guidance to identify such patient. Also, if a

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patient population with the "disease symptoms" are identified, the onset of disease has taken place, thus the pathology cannot be prevented (only further progression may be stopped). Further, because there is inadequate guidance as to the nature of the invention, it is merely an invitation to the artisan to use the current invention as a starting point for further experimentation for preventing destructive joint disease associated with rheumatoid arthritis by administering IFN- $\alpha$  orally. Lastly, because there are no working examples provided describing prevention of diseases or models it would require an undue amount of experimentation to one of skill in the art to practice the claimed invention.

The Office agrees with the Appellant that Shiozawa reference does not mention destructive joint disease. However, Shiozawa et al. reference was introduced to disclose the administration of interferon alpha to treat rheumatoid arthritis (Table II, page 406). The reference also taught that interferon-alpha therapy improves certain inflammatory indices of rheumatoid arthritis such as the joint score, C-reactive protein value and platelet count (p.406, column 2) and reduction in swelling (inflammation). Although, Shiozawa does not explicitly treat destructive joint disease, the treating of rheumatoid arthritis will treat destructive joint disease associated with rheumatoid arthritis because it is treating the same patient population. It is also noted that the Office did not claim that Shiozawa to be a complete authority on rheumatoid arthritis. Thus, this reference in combination with the lack of guidance in the instant specification provides sufficient, reasonable, specific or technical reasons to question enablement under 35 U.S.C. § 112. Therefore, the Office has met the initial burden under MPEP §

2164.04 [R-1] to establish a reasonable basis to question the enablement with acceptable evidence or reasoning.

### **3. The Claims, Properly Construed Are Enabled for the Identified Population**

Appellant argues that in view of the distinction between destructive joint disease and rheumatoid arthritis, and the identification of potential patients in the claims there is no reason for questioning the enablement and the Office has not met the burden. Specifically, the Appellant alleges that the Office argument that (1) the specification does not identify a patient population selected for preventing destructive joint disease, and (2) if a patient population was identified with disease symptoms then onset of the disease has already taken place, thus disease prevention cannot be attained provides no basis to question the enablement. Appellant also alleges that this shows an apparent misunderstanding of Appellant's invention, specifically, the difference between destructive joint disease and rheumatoid arthritis. Appellant asserts that rheumatoid arthritis patients can be identified that do not yet have destructive joint disease, and only prevention of destructive joint disease as claimed need to be enabled. Appellant asserts that Example 37 explains that a certain fraction of the patients will develop destructive joint disease and oral interferon alpha therapy targets prevention of the destructive phase of rheumatoid arthritis (page 85, lines 17-23). Appellant further claims that instant claim 1 (incorrect number, correct claim number is 19) is drawn to a method of preventing destructive joint disease associated with rheumatoid arthritis in a human individual with an earlier stage rheumatoid arthritis. Appellant also argues that the

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specification teaches that "Early treatment of rheumatoid arthritis with ingested interferon alpha prevents or retards progression of rheumatoid arthritis" (see page 86, lines 11-13). Thus, Appellant asserts that a target patient population in the claims and the specification has been identified. That is, rheumatoid arthritis sufferers who have not yet reached the destructive phase of rheumatoid arthritis (destructive joint disease). Appellant asserts that the specification makes it clear that other phases (besides destructive) of rheumatoid arthritis exist, and at least some phases or stages of rheumatoid arthritis occur before the onset of destructive joint disease. It is further alleged that the specification also teaches a patient having an early stage rheumatoid arthritis but not suffering from destructive joint disease can be identified and treated with interferon alpha to prevent the destructive phase from ever occurring. Thus, Appellant claims that there is no basis to question the enablement and the Office has not met the burden.

Contrary to Appellants assertions, the specification teaches only that a portion of rheumatoid arthritis patients will develop destructive joint disease (page 85, lines 17-19). However, there is no guidance to identify this portion of the patient population. Although, claim 19 refers to an individual with an earlier stage of rheumatoid arthritis for preventing destructive joint disease the instant specification provides no clear guidance to identify such patient (earlier stage). Do you treat all rheumatoid arthritis patients early with the hope of preventing destructive joint disease because if a patient population with the "disease symptoms" are identified, the onset of disease has taken place, thus the pathology cannot be prevented (only further progression maybe



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stopped)? Although, the specification teaches that the early treatment of rheumatoid arthritis with ingested interferon alpha prevents or retards progression of rheumatoid arthritis (see page 86, lines 11-13), there is no disclosure about preventing develop destructive joint disease. Contrary to Appellants assertion that the specification makes it clear that other phases (besides destructive) of rheumatoid arthritis exist, and at least some phases or stages of rheumatoid arthritis occur before the onset of destructive joint disease, there is no guidance provided in the instant specification to identify the various stages or phases. For example, there is no guidance as to what clinical indices of rheumatoid arthritis such as joint score, C-reactive protein values and platelet count maybe used to initiate the treatment (also follow the clinical progress) for the prevention prior to the onset of destructive joint disease. With respect to Appellant's allegation of an apparent misunderstanding of the instant invention, specifically, the difference between destructive joint disease and rheumatoid arthritis, the Office is interpreting the claims as a method to prevent the destructive joint disease which has a late onset that is associated with rheumatoid arthritis. Therefore, the position of the Office is that it has met the initial burden as required under MPEP § 2164.04 [R-1] to establish a reasonable basis to question the enablement with acceptable evidence or reasoning.

#### **4. Adequate Examples and Guidance Are Provided**

Appellant asserts that one of skill in the art need only apply the teaching in examples 36 and 37 specifically to early stage rheumatoid arthritis patients to practice the invention (see appeal brief page 13, 1<sup>st</sup> paragraph). Specifically, Appellant asserts that example 36 demonstrates the results of an open label phase I study of orally

ingested IFN- $\alpha$  in the treatment of patients with clinically stable rheumatoid arthritis. The compilation of results in Table 2 show that in 3 of the 4 patients treated there was substantial improvement in clinical disease indicia. It is further asserted that, example 37 describes, "a trend toward inhibition of CD3- and Con A-mediated IL-1, IL-6, and IL-8 secretion after eight weeks," of treatment with orally ingested IFN- $\alpha$  (see specification, page 84 lines 6-9). Appellant asserts that considering a reduction of inflammatory cytokine production can prevent progression of rheumatoid arthritis; example 37 clearly provides enabling support for Applicant's claims (see specification, page 85 lines 2-16 and page 86 lines 11-13).

Contrary to Appellant's assertion that there is adequate guidance provided in the specification there is no guidance provided in the specification (see above paragraphs B.2-B.4). Although, example 36 demonstrates that interferon alpha administration reduces, for example IL-8 secretion in some patients, there is no evidence in the specification or the prior art to indicate that the administration of interferon alpha prevents destructive joint disease associated with rheumatoid arthritis in an individual. While there was substantial improvement (via halting of progression) in terms of both joint pain and joint swelling, there is no evidence for preventing destructive joint disease associated with rheumatoid arthritis. Similarly, the example 37 indicates "a trend toward inhibition of CD3- and Con A-mediated IL-1, IL-6, and IL-8 secretion after eight weeks," of treatment with orally ingested IFN- $\alpha$ . However, none of these indices are correlated with destructive joint disease prevention. In fact these indices are related to the management rheumatoid arthritis. It is also noted that the sample size in these studies

is small and there is no statistical analysis with the observations provided. Thus, the Office maintains that the Appellant has not provided sufficient examples, guidance, and direction to enable the invention without undue experimentation as required in MPEP § 2164.01(a). Thus, for reasons set forth above the rejection of claims 19-22 under 35 U.S.C. § 112, first paragraph, scope of enablement should be maintained.

### **C. Under KSR, the Claims Are Not Obvious**

Appellant argues the rejection of claims 19-26 under 35 U.S.C. 103(a) as being obvious over Shozawa et al. (1992) in view of Cummings (U.S. Patent No: 4, 497, 795) and Cummings (U.S. Patent No: 5, 019, 382) and claim 27-30 as obvious over the combination of references above, further in view of Aman et al. (1994) spanning pages 13-21 of the Appeal Brief. Appellant is arguing that the Office has failed to show that Appellant's claims are obvious in view of the prior art. (see M.P.E.P § 2143.03).

#### **1. Graham Factors: The Scope and Contents of the Prior Art**

The Office takes no position on Appellants discussion of the instant claims. Appellant summarizes the teachings of the references. The summary of Shiozawa reference is not accurate. Contrary to Appellant's assertion that the Examiner (Office) conceded that Shiozawa does not teach the prevention of destructive joint disease (citing page 7 of the final rejection), the Office on page 7 of the final rejection stated that "Shiozawa et al. (1992) reference was introduced in the Office Action dated 4/12/2007 (page 7) to teach the teaching of administering IFN- $\alpha$  to treat rheumatoid arthritis (treatment of rheumatoid arthritis will inherently treat destructive joint disease associated with rheumatoid arthritis)". Further, the Office indicated on page 7 of the

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final rejection that Contrary to Appellant's assertion that the references individually do not teach the instant invention, the combined teaching does teach the instant invention of preventing destructive joint disease associated with rheumatoid arthritis by administering IFN- $\alpha$  orally as indicated in the Office Action dated 4/12/2007 pages 7 and 8. Although, the Appellant asserts that Shiozawa reference does not consider or evaluate interleukin levels in rheumatoid arthritis patient, or inflammation associated with rheumatoid arthritis, Shiozawa teaches that cytokines such as IL-1, IL-6 and TNF alpha play a important roles in the in the pathogenesis of rheumatoid arthritis, and the immunomodulation of the action of these cytokines may influence the activity of the disease (see page 405).

Contrary to Appellants assertion that the conversion from I.U. to units in '382 patent is relevant only to that particular invention, '795 patent also discloses that "as used herein, a "unit" of interferon shall mean the reciprocal of a dilution of interferon-containing material that, as determined by assay, inhibits on-half of a challenge virus plaque, the challenge virus being the vesicular stomatitis virus (VSV)" (see column 4, lines 55-68). This definition for units is identical to that disclosed in '382 patent (see column 3, lines 45-56).

Cummings '795 was included to teach the oral administration of 5,000 to 50, 000 units of interferon per Kg body weight.

## **2. Graham Factors: Ascertaining the differences between the prior art and the claims in issue**

### **a. The Differences Between the Claims and Prior Art Are Great**

Appellant argues that the Office position that treatment of rheumatoid arthritis as described by Shiozawa will inherently treat destructive joint disease is not true because only a certain portion of rheumatoid arthritis patients will develop destructive joint disease. In addition, Appellant asserts that the reference does not recognize destructive joint disease or a destructive phase of rheumatoid arthritis. Appellant contend that obviousness cannot be predicted on what is not known at the time an invention is made, regardless of whether a certain feature is later deemed inherent (see M.P.E.P § 2143.02). Appellant refers to In re Rijckaert, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir.1993).

Appellant also argues that patients studied by Shiozawa were also taking other medications, thus cannot teach the treatment of anything that could also be treated by these other drugs. Thus, it is asserted that Shiozawa reference cannot teach the treatment of anything that could also be treated by these other drugs. However, it is asserted that the instant claims reduce rheumatoid arthritis-associated inflammation and prevent rheumatoid arthritis- associated destructive joint disease. Appellant asserts that after comparing the differences between the cited art and the claims at issue it is clear that Shiozawa reference is irrelevant.

While it is true that only a certain portion of rheumatoid arthritis patients will develop destructive joint disease and Shiozawa does not discuss or recognize destructive joint disease, Shiozawa treats the same patient population as in the instant invention. Although, Appellant argues that this treatment not true they do not provide any evidence to contradict this position. The instant invention is drawn to preventing

destructive joint disease associated with rheumatoid arthritis by administering interferon alpha in humans at an earlier stage and Shiozawa reference treats the same population with interferon alpha. Thus, treating rheumatoid arthritis with interferon alpha will inherently prevent destructive joint disease. Contrary to Appellant's assertion that the obviousness cannot be predicted on what is not known at the time an invention is made, claimed element of treating rheumatoid arthritis with interferon alpha was known in the prior art. Furthermore, the fact pattern of the case cited by the Appellant and of the instant rejection is significantly different, and the court decisions are not binding with regard to the instant rejections. For example, In re Rijckaert, the U.S. Court of Appeals Federal Circuit reversed the obviousness rejection because inherency was based on what would result due to optimization of conditions and not what was necessarily present in the prior art.

Although, Appellant argues that patients studied by Shiozawa were also taking other medications and thus cannot teach the treatment of anything that could also be treated by these other drugs. This assertion is not true because Shiozawa clearly teaches the effect of interferon alpha on the patients by using placebo controls to differentiate the effect interferon alpha on rheumatoid arthritis (see Tables I-III). In addition, language of the instant claims also contains comprising language and thus could include other reagents along with interferon alpha. Thus, Shiozawa reference is relevant to the instant invention.

**b. The Modifications Render the Prior Art Unsuitable**

Appellant argues that '795 patent addresses appetite stimulation and there is no reason a person skill in the art would read the '795 patent and believe oral administration of the described animal appetite stimulant could be applied to humans because the patent teaches that interferon has opposite effect on humans. Appellant asserts that the '795 patent clearly states that interferon causes nausea and appetite loss when administered to people (column 3, lines 32-38). Thus, it is asserted that there is no suggestion to combine the human patient element of Shiozawa with '795 patent.

Contrary to Appellant's assertion, Cummings '795 patent was introduced to teach the oral administration and dosage (Office Action dated 4/12/2007, page 8). '795 patent also discloses clinical uses of interferon alpha in humans (column 2). Thus, the suggestion to combine the teachings of '795 patent with Shiozawa reference. In addition, courts have held that it is not necessary that the claimed invention be expressly suggested in any one or all of the references to justify combining their teachings; rather the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art, In re Keller, 642 F.2d 413, 288 USPQ 871 (ccpa 1981).

### **c. Aman's Self Contradiction Eliminates Its Suggestive Power**

Appellant contends that Aman reference is self contradictory and discredits itself. It is asserted that no person of skill in the art would read Aman's description of a phenomenon reported in certain tissue cultures, but reported as absent in others, and believe one of those results, but not the other, would translate into a drug therapy for humans suffering from rheumatoid arthritis.

Contrary to Appellant's assertion the complete reading of Aman reference teaches that interferon alpha substantially inhibits the production of cytokines including IL-1 and IL-8 (pages 4142, 4147 and abstract). It also discloses the anti-inflammatory role of interferon alpha. The Office has weighed the suggestive power of the reference and based on these facts finds the Aman article would not have deterred one of ordinary skill in the art from using it in the instant invention of reducing a level of an interleukin in a human individual with rheumatoid arthritis (see M.P.E.P § 2143.01 [R-6])).

**3. No Proper Rationale Supporting Obviousness is Provided: The Examiner's Burden is Thus Not Met**

Appellant asserts that the Office has not demonstrated the existence of the claimed elements in the prior art. It is also argued that the Office has failed to articulate a reason for combining the prior art, thus the burden of showing prima facie obviousness is not met. Specifically, Appellant asserts that Shiowaza reference does not inherently teach treatment of the conditions treated by instant invention, and there is no reason to believe that interferon alpha is responsible for whatever Shiowaza may treat considering the other medications taken by the studied patient population. It is also asserted that '795 patent does not teach or suggest oral administration of interferon to humans to treat rheumatoid arthritis. Thus, it is asserted that the elements of treating joint disease by oral administration are not taught. Appellant argues that there is no proper reasoned basis justifying the legal conclusion of obviousness of claims 19-26. Similarly, Appellant contends that for all the reasons stated above, no proper rationale



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supporting obviousness is provided for claims 27-30. Appellant contends that Aman reference is self contradictory and does not support an obviousness rejection of claims 27-30. Therefore, Appellant requests the reversal of the rejection of all claims under 35 U.S.C. 103(a).

The instant invention is drawn to preventing destructive joint disease associated with rheumatoid arthritis by administering interferon alpha in humans at an earlier stage and Shiozawa reference treats the same population (rheumatoid arthritis patients) with interferon alpha (see 2a above). Thus, providing the rationale for treating rheumatoid arthritis patients with interferon alpha will inherently prevent destructive joint disease. Although, Appellant argues that patients studied by Shiozawa were also taking other medications and thus cannot teach the treatment of anything that could also be treated by these other drugs. This assertion is not true because Shiozawa clearly teaches the effect of interferon alpha on the patients by using placebo controls to differentiate the effect interferon alpha on rheumatoid arthritis (see Tables I-III). While it is true that '795 patent does not teach or suggest oral administration of interferon to humans to treat rheumatoid arthritis, it does teach the oral administration and dosage (Office Action dated 4/12/2007, page 8, see also 2b above). '795 patent also discloses clinical uses of interferon alpha in humans (column 2). Thus, the suggestion to combine the teachings of '795 patent with Shiozawa reference. In addition, courts have held that it is not necessary that the claimed invention be expressly suggested in any one or all of the references to justify combining their teachings; rather the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art, *In*

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*re Keller*, 642 F.2d 413, 288 USPQ 871 (ccpa 1981). Therefore, providing the rationale to one of skilled in the art to combine the references to reject claims 19-26 under 35 U.S.C. 103(a) as being obvious over Shozawa et al. (1992) in view of Cummings (U.S. Patent No: 4, 497, 795) and Cummings (U.S. Patent No: 5, 019, 382).

Although, Appellant contend that the Aman reference is self contradictory and does not support an obviousness rejection of claims 27-30, Aman reference teaches that interferon alpha substantially inhibits the production of cytokines including IL-1 and IL-8 (pages 4142, 4147 and abstract). It also discloses the anti-inflammatory role of interferon alpha (see 2c. above). Thus, providing the rationale to combine the references to reject claims 27-30 under 35 U.S.C. 103(a) as being obvious over Shozawa et al. (1992) in view of Cummings (U.S. Patent No: 4, 497, 795) and Cummings (U.S. Patent No: 5, 019, 382) further in view of Aman et al. (1994).

**(11) Related Proceeding(s) Appendix**

Copies of the court or Board decision(s) identified in the Related Appeals and Interferences section of this examiner's answer are provided herein.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Jegatheesan Seharaseyon

/Jegatheesan Seharaseyon/  
Examiner, Art Unit 1647

June 19, 2008

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Conferees:

Christine Saoud

/Christine J Saoud/

Primary Examiner, Art Unit 1647

Manjunath Rao

/Manjunath N. Rao, /

Supervisory Patent Examiner, Art Unit 1647

Janet Andres

/Janet L. Andres/

Supervisory Patent Examiner, Art Unit 1625